

ON
THE THERAPEUTICAL ACTION OF MEDICINES
IN
DILATED CONDITIONS
OR
T H E B L O O D V E S S E L S.

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THE THERAPEUTICAL ACTION OF MEDICINES

IN

DILATED CONDITIONS OF THE BLOODVESSELS.

IT is admitted by all practical physicians, that the science of therapeutics is in a most unsatisfactory state. A brief glance at the immense variety of conflicting opinions entertained regarding the best mode of treating disease, is sufficient to convince every intelligent mind that the whole subject is in utter confusion. It is only necessary to compare the various recommendations for the treatment of but a single disease, made by those authors who have written on it, in order to be satisfied that very little is known of the remedies for our bodily infirmities. It is still a standing reproach on the profession, that after centuries of careful observation and experiment so little progress should have been made towards those great objects of medicine,—the relief of suffering, and the prolongation of human life. Chemistry, physiology, and pathology have made most rapid advances, but therapeutics seem to be at a stand-still. It is true, progress of a certain kind has been made. A school of men has arisen, of which Professor Bennett of Edinburgh is one of the principal exponents, who trust almost entirely to the powers of nature in the cure of diseases. Founding their opinions on the well-known teaching of experience, that medicines, in their present mode of administration, do not, as a rule, exert any remediable influence on disease, they conclude that diseases always run a natural course, and cannot be modified or controlled by any medicinal agent whatever. Among the immense number of powerful agents found in nature, they believe that few have yet been discovered which will exercise a curative effect on the maladies of the human frame. These views are rapidly gaining ground, and are embraced by perhaps the greater number of physicians at the present day. The drugging system has been abandoned, and the natural system resorted to,—of feeding nature, and allowing nature to look after itself. There is thus progress made, in a way, towards the better

treatment of disease. I say, in a way, because it is not true scientific progress. It is merely the abandonment of the system of doing too much—the *nimia diligentia*—for the adoption of the system of doing little or nothing. Of the two, certainly the natural system is to be preferred. It allows nature to exercise her own undoubted powers unchecked, and thus contributes much more surely to the welfare and recovery of the patient. Should the case terminate fatally, the patient dies at least a *natural* death. But still, it is not scientific progress. It is a reaction from over-credulity to overscepticism, from the belief in the absolute necessity of medicines to a conviction of their absolute uselessness. If we contrast the position of our forefathers, and their vast array of drugs, with our own present helpless position—standing with folded arms at our patient's side, doing little more than announcing the name of his disease, and giving daily bulletins of its course—we will be little inclined to consider our progress very satisfactory.

The conclusion on which the followers of the natural system seem to proceed is, that there are few agents yet discovered which will exert a true remediable influence on disease. The oft-repeated, almost invariable failures met with in practice, and the discrepancy among observers regarding the action of drugs, seem to give colour to that opinion. It is impossible to look back over the recorded experience of the last fifty years without being in a considerable degree inclined towards more or less complete disbelief in medicinal agency. That period has witnessed the rise and fall of a whole dynasty of medicines, each one more vaunted and promising more fair than its predecessor, but all destined more or less to fall into disuse. It cannot be wondered at, then, if the rising generation of medical men should declare themselves sceptics. Yet, notwithstanding the great uncertainty of medicinal action, it has long appeared to me that the conclusions on which the natural system of therapeutics is based, are premature. They proceed on the assumption that our knowledge of disease and of medicinal action on the living body, is sufficiently perfect to warrant an accurate determination of the influence exerted by the one over the other. To be sound, they ought to be based on a thorough acquaintance with Pathology on the one hand, and of Materia Medica on the other. It is needless to say how far short we are of this perfection. Rapid as has been the advance of pathology, and clear as is the light it has shed on many obscurities, we must, nevertheless, confess our ignorance of disease in its true nature and causation. The state of the Materia Medica is not much better. Although many drugs have been familiar to the profession for centuries, and although an infinite number of experiments of almost every kind have been made with them, both on man and on the lower animals, there is still great discrepancy regarding their properties. The diversity of opinion is not so much in regard to their physiological or toxic properties; on the contrary, most writers are at one on the symptoms usually manifested in the

living body by each medicine. But it is when their application to therapeutics is considered, when their medicinal virtues come to be judged of, that great diversity exists. On this point there is scarcely any agreement. And moreover, old and apparently settled opinions on the properties of medicines are every now and then changing. Agents, which have long been prescribed in accordance with a given theory, are suddenly found to be possessed of different qualities, and their administration varies accordingly. This is remarkably so at the present time. Quinine, so long the fashionable tonic, the universal panacea for all sorts of debility, is already regarded with doubt. Digitalis, belladonna, iron, even opium itself, are the objects of suspicion, and the subjects of new trials. And it would not be surprising if the fabrics raised by time-honoured belief should crumble to pieces under the rude shocks of an age, the characteristic of which is to believe nothing and doubt everything.

Now, it may be asked, with good reason, When and where is this to end? Are we always to oscillate from side to side, without fixed principles, driven to and fro like the waves of the sea? Are we never to have decided opinions, but to go on as before, disbelieving or doubting to-morrow what we believe to-day, rendering ourselves and our profession the laughing-stock of an intelligent public? It is to be hoped not. There are even now signs of a change; and I venture to predict that before long, very many of the questions which now disturb and distract us will be definitely settled on a fixed basis. But whatever may be the future of therapeutics, it is certainly premature, in the face of present diversities, to accept and act upon the conclusion that disease is irremediable by medicinal agency. The proper course is evidently to undertake a careful re-examination of the whole subject—to begin, as it were, at the beginning, and, with the additional knowledge afforded by the progress of the collateral sciences, endeavour to procure accurate results. A long-continued course of persevering investigations could not fail to be productive of very important practical benefit.

In endeavouring to afford some little help towards the elucidation of this very important subject, I may premise that observers, in studying the action of medicines, appear to have fallen into two mistakes, both of them insignificant at first sight, but leading to serious fallacies. The first mistake consisted in drawing inferences as to the action of medicines on man, from the effects observed by experimenting with them on the lower animals; and the second, in regarding the symptoms produced in the human economy as the only and invariable physiological phenomena characteristic of the substances ingested.¹ It is scarcely necessary to bring forward proofs of the many fallacies to which the first error leads. The want of correspondence between the properties manifested by certain substances when administered to animals, and those exhibited in

¹ I find that I am anticipated in this remark by Brown-Séquard, in his admirable lectures.—*Lancet*, 10th March 1866, p. 248.

man, is admitted on all hands. The habits and mode of life of animals being so diverse from those of man, no proper comparison can be made between them. Some animals are uninfluenced by agents which destroy human life. The information, therefore, derived from this source, however valuable in itself, is by no means a trustworthy indication of medicinal action. The second error is a very natural one, and, in the circumstances, almost impossible to avoid. That the physiological symptoms of a medicine, repeated invariably whenever it was administered, should be regarded as its only action, was merely what might be expected. It could scarcely be otherwise. Yet it was an error, and has proved itself to be so, by the very fact, that there still exist conflicting theories as to the therapeutical value of those medicines, regarding whose physiological properties mostly all are agreed. It is my object, in this and following papers, to show that medicines have another and a very different action on the economy from what their physiological symptoms would lead us *à priori* to suppose they had.

If we carefully examine the fundamental nature of diseases in general, we cannot avoid noticing the singular uniformity as to origin which prevails among them. Widely different as are the ultimate results, and varied as are the mechanical and chemical changes induced in the body, it is possible, nevertheless, to trace upwards the various stages of disease, until we arrive at what appears, so far as we know, to be its common centre, from which it derives its origin. It matters not what names we give to diseases. We may call them by as many names as we choose, until Nosology be a complete dictionary; but all arise, if our pathology be correct, from the same centre. This centre is the joint cerebro-spinal and vaso-motor nervous systems. The latest physiological and pathological researches warrant us, I think, in laying down the proposition—that most diseases are due to a morbid state of the nervous system, which morbid state either arises in the nervous system itself, or is induced by the presence of a noxious element in the blood. Few, I suppose, will question this proposition. Disease has many forms and produces many changes, but the first step in the downward direction is derangement of the nervous influence, whether cerebro-spinal or vaso-motor. It is, then, of the greatest importance to determine the nature of this derangement; for if we can do so, we make great progress towards a proper understanding of the treatment to be pursued.

In following out this subject, I intend to confine myself on the present occasion to the consideration of those morbid conditions which are attended by dilatation of the blood-vessels. I shall enter into some details regarding the origin of inflammation, a condition occupying so prominent a place in the production of disease, and hope to demonstrate that the course of the inflammatory process is precisely analogous to the effect of medicines on the system. The therapeutical action of medicines will then be more clearly understood.

Inflammation is, then, as I understand it, primarily and essentially a disorder of the nervous system. The stagnation of blood, the effusion of lymph and serum, the suppuration, etc., which are commonly identified with inflammation, are themselves only the result of deeper seated morbid processes affecting conjointly the cerebro-spinal and vaso-motor nervous systems. The researches of Bernard and Brown-Séquard on the nervous system have brought to light the very important part which nervous influence plays in the production of inflammation. These writers, as well as others, have shown that if the cervical sympathetic be irritated, certain changes take place in the parts to which it is distributed. These changes are summed up by Brown-Séquard as follows :—

1. Contraction of Bloodvessels.
2. Diminution of Blood.
3. Decrease of Vital Properties.

On the other hand, if the same nerve be simply divided, the opposite condition takes place, namely—

1. Dilatation of Bloodvessels.
2. Afflux of Blood.
3. Increase of Vital Properties.

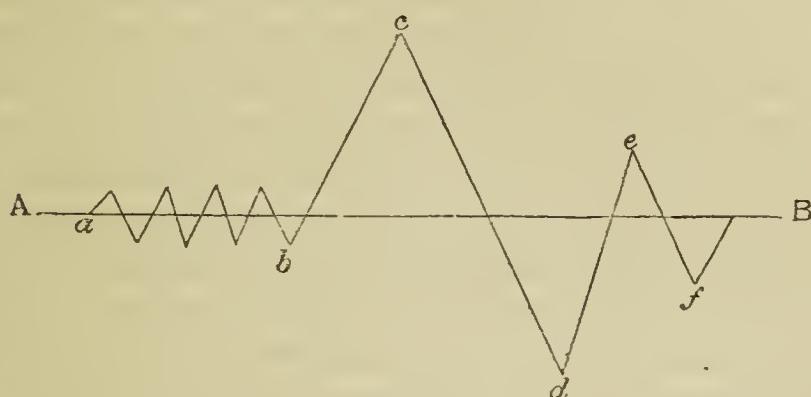
In the first case, the vaso-motor nerve has been excited or stimulated; in the second, it has been paralyzed. Here is, then, a miniature portrait of inflammation. It will be seen that the effects of paralysis of the sympathetic bear a close resemblance to the state of parts in the inflammatory process. In that morbid condition there exist enlargement of the bloodvessels, with consequent increase in the quantity of blood, and greater activity of the vital properties of the tissues, all of which are closely similar to the results of division of the sympathetic. There can be little doubt, therefore, that this nerve exercises considerable influence in the production of inflammation. But this is not all. There seems, in order to constitute a true phlogistic action to be another influence at work, that of the cerebro-spinal system, which operates in a manner hitherto unexplained; and, moreover, Lister's experiments prove that, along with derangement of the combined nervous influence, there are local changes in the affected part. There is what is called a suspension of the concurrent exercise of function among the minute elements of the tissues of the organs involved. Thus, three factors enter into the composition of inflammation. There is first, paralysis of the vaso-motor nerves; secondly, derangement of the cerebro-spinal influence; and, thirdly, suspension of molecular function. Among them, however, there seems good reason for concluding that the chief place is taken by the vaso-motor nerve. Whatever part may be played by the cerebro-spinal nerves, I am inclined to think that it is secondary in point of importance to that of the sympathetic. It is true that the two systems are mutually dependent on each other. The vaso-motor derives its influence from the cerebro-spinal, while the latter, on the other hand, is dependent on the vaso-motor for the due

transmission of its supply of blood. It would appear, also, from the experiments of Claude Bernard, that while the sympathetic system regulates the supply of blood to the various organs of the body, the cerebro-spinal determines the character of the nutrition. For example, when the skin is wounded, repair seems to be effected by the combined influence of the two great divisions of the nervous system which we are considering. Blood is sent to the wounded part by the vaso-motor nerves, while the particular organization formed from the blastema is determined by the cerebro-spinal nerves. I am aware that an opinion has lately been started to the effect that the cerebro-spinal and vaso-motor systems are antagonistic; but I think it has been advanced without good cause. It rests only on the apparent anomaly that, in Bernard's experiments, section of the cervical sympathetic was followed, not by an increase of the salivary secretion, as would *à priori* have been expected, but by a diminution; and that, conversely, irritation of the nerve was followed, not by diminution, but by increase of the saliva. On these experiments rests the theory of the antagonism of the two great nervous centres. The anomaly, however, is more apparent than real; and, had I time, I might give a satisfactory explanation of it, as well as of another, which is, that the paralyzing influence of belladonna on the cervical sympathetic is attended by dilatation of the pupil, when we would have expected contraction. These anomalies, however inexplicable, are insufficient to establish any proof of antagonism between the cerebro-spinal and vaso-motor systems; and, in the meantime, we are forced to regard both these systems as mutually dependent, acting simultaneously in health, and affected conjointly in disease. In inflammation, they both suffer, the vaso-motor probably being first involved.

Now, it is of the highest importance to determine, as far as possible, the first step in this nervous derangement. And here it is that, in my estimation, a serious oversight has been made, leading to very erroneous practice. It is commonly supposed that the paralysis of the sympathetic on which inflammation in great measure depends, is the *primary* effect of the exciting cause; whereas, in truth, it is its *secondary* effect. The first action of all those causes which tend to produce inflammation in the body is to stimulate and excite the vaso-motor nerves, the result of which is the contraction of bloodvessels, decrease of blood, and of vital properties, which, as we have seen, follow galvanization of this nerve in animals. This state of excitement is followed, as a natural and necessary consequence, by a *reaction* to the opposite state of paralysis, with those local changes which result therefrom, as seen also in animals after division of the sympathetic. Thus, inflammation, as observed in the body, is a reaction from a previous and often invisible stimulus upon the vaso-motor system. Let me explain this a little more clearly.

The vaso-motor system in health may be compared to a balance

moving gently upwards and downwards, never rising too high, nor falling too low. To illustrate this, let the straight line A B, in the accompanying diagram, represent the vaso-motor system when exactly midway between excitement and paralysis; in other words, the state of the bloodvessels when midway between contraction and dilatation. The zig-zag line *ab* will represent the variable condi-



tion of the vaso-motor system. The alternation of rising and falling represents the alternate state of excitement and depression which constitutes the healthy condition. This variation is essential to health. In fact, all the functions of the body depend on it. When food is taken into the stomach, its presence there produces excitement of the vaso-motor nerves, followed almost immediately by reaction and determination of blood to the viscera, whereby, along with cerebro-spinal influence, the secretion of gastric juice is effected. When the body is thrown into active exercise, there is a certain amount of heat generated by friction and other causes, and this heat acting primarily as a stimulant, induces reaction to what, for convenience sake, I shall call a healthy paralysis of the sympathetic, creating that activity of the circulation and comfortable feeling of warmth which are so familiar to us all. A cold bath acts in a similar way. And numberless instances might be mentioned, showing that upon this singular alternation of stimulus and reaction the wellbeing of the economy is greatly dependent. If the vaso-motor system were fixed invariably in the middle position indicated by the line AB, it would no more resemble an elastic band adapting itself to circumstances, or a watch spring in its regular oscillations, but would be rigid and motionless. In such a case, digestion would be at a stand-still. The quantity of gastric juice poured forth in a given time would be insufficient for the solution of the food necessary to nutrition. We should be unable to endure the heat of summer, or the cold of winter, much less the hourly vicissitudes of temperature to which we are exposed. But nature provides for these changes by endowing the vaso-motor system with a degree of elasticity which, within certain limits, enables it to adapt itself to the various conditions of the body. Now, suppose the stimulus to be too strong. Suppose the line *ab* to be acted upon by a force stronger than usual, such as intense cold, and is pulled higher than is consistent with health, say to a point *c*, which represents spasm

of the bloodvessels, the necessary consequence is, that, when the force has expended itself, the reaction will be proportionally excessive, and the line will fall lower than usual, say to *d*. The point *d*, then, will represent inflammation as manifested to our senses by its ordinary symptoms. The condition indicated by the point *c*, that of excitement, is often invisible, or at least unnoticed, and can only be presumed to have existed from the appearance of the opposite state of reaction. It has not received the attention it deserves, but it is, nevertheless, the primary and essential step of the whole morbid process. Inflammation cannot take place without it, for, as I shall hereafter show, all these causes which induce the inflammatory state, act primarily as stimulants of the vaso-motor system. A very simple experiment will place this in a clear light. If ether spray be directed on the skin by means of Dr Richardson's apparatus, the effects of the intense cold will be seen by the naked eye. All the symptoms of galvanization of the sympathetic which I mentioned a little ago, are at once observed, namely, contraction of bloodvessels, diminution of blood, and decrease of vital properties, manifested by whiteness and insensibility of the part. When the stimulus is removed, reaction gradually takes place till the parts resume their natural appearance; but it does not stop there. It goes beyond health, and approximates disease. The surface is congested—there is dilatation of the bloodvessels, more blood, and more vital energy, as increased heat and sensibility, than are found in the ordinary state. And if the cold were applied for a sufficient length of time, stagnation, with its consequences, would doubtless follow. I need scarcely refer to the familiar example of what takes place in the web of the bat's wing or frog's foot under the microscope, when pricked with a needle or touched with a drop of alcohol. It has long been known that the first effect of the stimulus is to contract the vessels, to be followed by their dilatation and stagnation of blood. Such is exactly the course of inflammation. Cold, or some other agent, first of all stimulates the vaso-motor system, causing spasm of the bloodvessels. Simultaneously with this, and perhaps in consequence of it, there is derangement of the cerebro-spinal influence, and suspension of the concurrent exercise of function among the minute elements of the tissues. Then follows reaction, proportionate in intensity to the previous stimulus, paralysis of the vaso-motor system takes place, causing dilatation of the blood-vessels, with all those local changes in succession which constitute the inflammatory state.¹

In thus endeavouring to explain the origin of inflammation, it is not to be understood that I am underrating the influence of the

¹ "When bloodvessels in the ear and face of a dog are made to contract considerably by a very powerful galvanic excitation of the cervical sympathetic nerve, we find that, after a short time, they become exhausted and paralyzed, and that, consequently, they dilate as much as when their motor nerve is divided and paralyzed."—Brown-Séquard, *Lancet*, 10th March 1866, p. 248, note.

cerebro-spinal system by giving so much prominence to the vaso-motor. On the contrary, I do not think that true *active* congestion can take place without previous disturbance of the cerebro-spinal influence. Paralysis of the vaso-motor nerves seems to go no further than passive congestion, at least, if the continuity of the nerve be gradually or gently interrupted. This was well seen in a case which I published in the *Medical Times and Gazette* of Nov. 11, 1865. In that patient, interruption of the functions of both cervical sympathetics was followed by intense *passive* congestion in the organs to which they were distributed, but there was no inflammation. I am, therefore, inclined to believe that, while the vaso-motor system takes the chief part, a concurrent derangement of the cerebro-spinal is requisite for the production of true inflammation. Perhaps, also, a good deal depends on the force and suddenness of the original stimulus; which, if severe, might tend to cause active congestion by the intense sudden reaction consequent.

Though not bearing directly on the object of this paper, I may here touch upon the febrile state which so often accompanies inflammation, and is called inflammatory fever. This febrile state is not due, as is often supposed, to an effort of the heart to overcome the obstacle offered by the local lesion to the passage of blood. If it were so, we should have inflammatory fever in every disease where there was an obstruction to the sanguineous current, which is not the case. We have, moreover, a condition bordering on fever, where we know there can be no such obstacle. During active exercise, the circulation is in a state closely allied to inflammatory fever. There must be another cause, therefore, for the febrile condition. That cause is the same stimulus which originated the inflammation. Let us look for a moment at the peculiar anatomical arrangement of the cardiac nerves. Between the brain and the abdomen extends a nervous circle, of which one segment is formed by the pneumogastrics, and the other by the cervical and thoracic sympathetics, the great and small splanchnic nerves. The two segments are connected above with the brain, and below with the chylo-poietic viscera. In the centre of this circle, which may be denominated the cerebro-ganglionic circle, lies the heart, and from the circumference are sent off a number of branches for distribution to that organ. The heart's action is thus directly controlled by the cerebro-ganglionic circle. Every impression communicated to the latter is felt by the former. Now, if a strong stimulus be directed on the nervous circle, such as cold from without, or a poison from within, it is thrown into a state of temporary excitement, causing those rigors and general depression which usher in a fever, and constitute its cold stage. The reaction from this is its hot or febrile stage. If the morbid action go no further, the fever subsides, and its subsidence is attended with perspiration, which is looked upon as a successful effort of nature to throw off the offending cause, inasmuch as it is attended with relief to the symptoms. But it is

rather a coincidence, and should be regarded as a concomitant sign that the nervous circle is recovering its equilibrium. Now, in the case of inflammation, if the original stimulus be comparatively weak, it will affect only the local nerves of the part involved, as, for instance, in coryza or tonsillitis, where there is often no attendant fever. But if the stimulus be powerful, it will not only act on the nerves of the inflamed organ, but will at the same time excite the nerves of the heart, causing decrease of the vital properties of the organ, and of blood in its tissue, manifested by chilliness, paleness of the surface, and general depression. Then comes reaction, proportionate to the intensity and duration of the previous stimulus, more blood is sent to the tissue of the heart in consequence of the paralysis of its nerves, there is an increase of its vital properties manifested by the greater frequency and force of its contractions, the functions of the economy are momentarily exalted, rendering the blood richer in fibrin—in a word, there is inflammatory fever. Thus, what was long considered an indication of increased power in the heart, is, in reality, only a sign of its weakness. The quicker and more strongly the heart beats, the more are its nerves paralyzed.

Having thus given a brief outline of the part played by the vaso-motor system in the incipient stages of inflammation, I have now to show that the action of medicines on the living body is precisely analogous. Whatever may be the ultimate effect of a substance, whether it be known as a purgative, a tonic, or a narcotic, its primary action is on the vaso-motor system. No doubt, in many cases there is a variety of secondary phenomena, as might be expected from the complexity of the organism, and it may sometimes be difficult to define the local origin of the symptoms; yet, when these symptoms are carefully analyzed, they will be found to possess a local origin at first. Dr Christison, in his work on poisons, says,—“Poisons have been often, but erroneously, said to affect remotely the general system. A few of them, such as arsenic and mercury, do indeed appear to affect very many organs of the body. But by much the larger proportion seem, on the contrary, to act on one or more organs only, not on the general system.” And further on he says,—“Some act chiefly by enfeebling or paralyzing the heart, others principally by obstructing the pulmonary capillaries, others by obstructing the capillaries of the general system, others by stimulating or depressing the functions of the brain or of the spinal cord, others by irritating the alimentary canal, others by stimulating one or another of the glandular organs, such as the salivary glands, the liver, the kidneys, or the lymphatic glands.” It is foreign to my purpose to inquire into the secondary or general effects of medicines; these may be accounted for in a variety of ways, and do not influence the matter on hand. But what I wish to point out is, that when the local effects of drugs are minutely examined, they will be found always to involve more or less the vaso-motor system, and to produce in it changes similar to, if not

identical with, those which occur in inflammation. The medicines themselves may be arranged under two heads: those which have no reaction after their stimulus on the nerves or spasm of the blood-vessels—the pure astringents, acting chemically on the tissues,—and those which, after their stimulant or spasmodic action has passed off, are followed by more or less reaction to paralysis of the sympathetic or dilatation of bloodvessels. To the latter class belong nearly all the contents of the *Materia Medica*. They possess the double property of stimulating and paralyzing the sympathetic,—in other words, of contracting and dilating the bloodvessels. Take the case of purgatives. A double action is universally ascribed to them, their purgative effects being usually followed by more or less constipation. But what I wish particularly to call attention to is, that, in accordance with the laws of inflammation, prior to their purgative action, and essential to it,—the cause of it, as it were,—there is a previous spasm of the bloodvessels, or excitement of the sympathetic, and that the subsequent purgation is in proportion to the intensity and duration of that excitement. We know well that laxative medicines act by creating irritation and inflammation of the mucous membrane of the intestinal canal,—an inflammation not to be distinguished from that which is called idiopathic. If, then, this idiopathic inflammation originate in the manner I have already described, as it undoubtedly does, it is but a natural inference to conclude, that purgatives operate in a similar way, and begin their action with spasm of the bloodvessels. Tonics, again, will in large doses irritate the stomach, from which we conclude that, as in the case of purgatives and emetics, their primary action on the bloodvessels is spasmodic. Narcotics also belong to the same category. Indeed, one of them, belladonna, is now recognised as having the double action which I am endeavouring to show belongs to medicines in general. Brown-Séquard, speaking of the remedial effects of belladonna, says,—“Most of these remedial effects are evidently due to a contraction of bloodvessels, as are also other effects, such as the stoppage of hæmorrhages, and of the mammary and salivary secretions produced by belladonna and the ergot of rye.” And then he goes on to say,—“A remedy can produce with different doses two opposite effects. Belladonna, for example, by its influence on the bloodvessels of the spinal cord, will diminish sensibility, the reflex faculty, the tendency to convulsions, etc.; but if the dose be toxic, there will be a morbidly increased sensibility, reflex faculty, and convulsions will occur.” . . . “A number of remedies may have quite opposite action in remedial and toxic doses.”¹ These remarks almost anticipate my paper, but I quote them in confirmation of the views I now inculcate, which I held before they appeared, and which I have worked out independently. It may be difficult at first sight to account for the varied action of narcotics on these principles. But when we consider that the brain is an aggregation into one organ of many separate and so far in-

¹ *Lancet*, 10th March 1866, p. 248.

dependent portions, and that each narcotic may have a special preference for one portion more than another, the difficulty vanishes. We know that the base of the brain consists of a number of distinct and separate ganglia, intimately connected, yet functionally independent, and that the spinal cord has its anterior, posterior, and lateral columns, and its central gray matter, each with its own function, though bound together in one organ. There is good reason also for concluding the cerebrum to be a congeries of separate organs. The singular affection called aphasia seems to show that the organ of articulate language is one small convolution on the left side of the cerebrum. Each convolution is probably a separate organ by itself, and the brain an aggregate of these organs. In all likelihood, therefore, each narcotic influences its own particular portion specially, implicating the others only through the intimate connexion which subsists between them. Now, when we examine the action of the best known narcotics, we find that one of the earliest manifestations of their toxic or poisonous properties is a congested state of the parts on which their influence is exerted. The poisonous action of belladonna, for example, is attended by dilatation of the bloodvessels of the face and head, and doubtless also of the brain. Opium also is attended with determination of blood to the base of the brain, and when its symptoms are fully developed, they are not to be distinguished from apoplexy of the pons Varolii. And whatever narcotic we examine, congestion is one of its prominent early characteristics. If, then, a dilated state of the bloodvessels of the brain, or its separate parts, be one of the first symptoms of a narcotic, the inference is plain ; there must have been a previous primary action of spasm or excitement of the vaso-motor nerves ; and narcotics would come under the same category as purgatives, tonics, and other medicines, having, like them, a double action on the vaso-motor system—first excitement, and then paralysis. Thus all the varieties of medicines are identical in their primary action ; the difference in their secondary effects being due, partly at least, to that particular portion of the sympathetic for which they severally have an affinity. Purgatives act on various divisions of the abdominal sympathetic, tonics on the solar plexus and cerebro-ganglionic circle, narcotics on the cervical sympathetic, diuretics on the renal nerves, and so on. Hence, it might be a legitimate question, whether those names which indicate only their secondary action might not with some propriety be abolished, and some such name as vaso-motor stimulant substituted. The term neurotic is rather vague, for, according to these views, all medicines are properly neurotic. A definite term expressing the primary and local effect of a drug would, at all events, convey to the mind a much better idea of its medicinal action than such names as purgative, narcotic, and the like—names which are too often made the groundwork for the purest empiricism, sometimes of erroneous practice.

It will not be out of place here to notice the singular analogy subsisting between the primary effects of medicines and those of fever poisons. As each medicine acts on its own portion of the sympathetic, so each fever poison implicates a particular part of the same system. The ultimate derangements may be, and are, very various; but the brunt of each fever falls on one division of the vaso-motor nerves. In typhus, for instance, the cervical sympathetic suffers. I have seen both nerves swollen to twice or thrice their usual size in fatal cases; and Dr Beveridge has, I believe, always found the same condition in the post-mortem examinations he has made. Enteric fever involves the abdominal sympathetic, the ganglia of which are found enlarged and softened. The other febrile diseases also have their favourite nidus. Curiously enough, too, they all commence their action by inducing spasm of the blood-vessels (cold stage), and the reaction from that indicates the particular disease present (febrile stage). These facts are most instructive. They show that the vaso-motor system is one, and that whatever agent operates on it, the effects are the same—excitement first, paralysis afterwards.

I come now to the practical application of the doctrines I have been inculcating. This part of the subject is so important, and offers so wide a field for investigation and experiment, that I beg to call special attention to it, the more so, considering the extensive part which inflammation and dilated conditions of the bloodvessels generally play in the production of disease. If, then, medicinal agents stimulate the vaso-motor system primarily (spasm of bloodvessels), and paralyze it secondarily (dilatation of bloodvessels), it may be supposed that inflammation being a paralysis of the same system, it would be aggravated by medicines in their ordinary physiological doses. Experience confirms this supposition. We find in practice that purgatives are injurious in, and aggravate diarrhoea; tonics and emetics increase pre-existing irritation of the stomach; narcotics are hurtful in congested states of the brain; diuretics in inflammation of the kidney. All this is true, supposing the medicines given in the usual prescribed doses of the Pharmacopœia. But if we concede a double action to medicines, if we admit that prior to their recognised effect on the economy, they have a spasmodic action on the bloodvessels, inducing their contraction, we will naturally inquire how this primary action may be turned to practical account. What I maintain is, that medicines given in very small doses when the bloodvessels are dilated (paralysis of sympathetic) will exert their primary action of contracting the bloodvessels (excitement of sympathetic), and no more. Their action will then cease; for whatever benefit is to be expected by administering medicinal agents in doses so small as to go no further than spasm of the bloodvessels, it will then be accomplished. This will be understood by a reference to the diagram, page 9. The point *d* is supposed to represent the state of paralysis to which the sympathetic has fallen from an oppo-

site state of excitement, *c.* It therefore represents the inflammatory state. Now, if we wish to raise the nerve to the level of health, we shall evidently gain our object by applying a stimulus to it. If we administer a medicine in a physiological or toxic dose, the stimulus will be too strong, the nerve will be raised as high or higher than before (*c*), and there would be a corresponding reaction to the old state (*d*), or even lower, representing an aggravation of the symptoms. But if a very small dose be given, so as to afford a comparatively weak stimulus, the nerve will be raised to a point considerably below that of its first excitement, say to *e*, and the reaction from this moderate excitement or vascular spasm would bring the nerve almost or altogether to a state of health, say to *f*, which is much higher than *d*, the inflammatory state. The therapeutical effect of a medicine is thus the reverse of its physiological action, at least in dilated conditions of the bloodvessels. If disease be attended with spasm of the bloodvessels, the usual physiological doses are properly indicated; but if the opposite condition exist, these doses do harm. A much smaller dose is therefore necessary. Now, the question is, How small must the dose be which is required to produce the stimulant effect without causing undue reaction? If one grain of a medicine induce both excessive stimulus and excessive reaction, what fraction of a grain will suffice for a moderate stimulus and reaction? This obviously can only be determined by experiment. On this subject I have been making observations for a considerable time. The limits of this paper forbid me to bring forward the results on the present occasion, but I hope hereafter to submit my experience in an extended form. I may state that my observations fully bear out the views I have been propounding, and that I have arrived at some very interesting and striking results. Care must be taken, however, not to draw inferences, as has hitherto been done, from the effects of medicines on the healthy body. To find out that five grains of aloes will purge, and thence to infer that the proper use of aloes as a medicinal agent is to purge, and that five grains is the dose, is an example of what I mean. This is the only result to be obtained by experimenting on the healthy economy.¹ Unfortunately, however, the whole present system of therapeutics is based on it. It is the secret of the confusion which exists in the profession regarding the medicinal treatment of disease. No idea of medicinal dose can be obtained by such means, although the observations are most valuable on other accounts. The primary stimulating action of drugs is in most cases invisible, when they are administered to a healthy subject. Cold is one exceptional agent. We can see with the naked eye, and appreciate by other means, both its effects. We recognise also the two primary effects of fever poisons. But with most drugs it is different. For the momentary contraction of blood-vessels in separate portions of the body cannot easily be taken cog-

¹ *Lancet, loc. cit.*

nisance of, either because they are too limited to produce appreciable symptoms, or because the healthy nerves cannot be influenced except by such doses as not only contract the vessels, but induce subsequent reaction. We are forced, therefore, to conclude in this way, that when such reaction exists, it must have been preceded by stimulus of the sympathetic (contracted bloodvessels). The case is otherwise when we come to experiment with diseased nerves, that is to say, with the paralyzed sympathetic (dilated bloodvessels). There the effects of a small dose are at once seen in the contraction of bloodvessels and restoration to the healthy state. How a minute dose should thus affect a paralyzed nerve, while it uninfluences it in its ordinary state, is a phenomenon we cannot explain. But that it does so, there can be no doubt. There seems to be a peculiar susceptibility to medicine manifested by the sympathetic in its paralyzed state. The same thing is witnessed by physiologists in animals. In Brown-Séquard's *Physiology and Pathology of the Central Nervous System*,¹ we find the following results described, among many others, as due to section of the sympathetic:—

“27. The first convulsions after poisoning by strychnia take place there.

“28. A galvanic current too weak to act on the other side may produce contractions there.”

From which experiments we conclude, that a dose of a medicine too weak to exert any action on the sound nerves, will operate on them when paralyzed. If we suppose strychnia to be primarily a stimulant to the vaso-motor system, it would, in the same manner as a purgative, aggravate a pre-existing paralysis of that system, shown by the increased vitality of the parts, and greater readiness to contraction of the muscles. But if a very small dose be administered, it would, by contracting the bloodvessels, remove those symptoms previously existing. All medicines act in a similar way on the nerves for which they severally have an affinity, the therapeutical dose being considerably smaller than the physiological, and only to be determined with accuracy by repeated experiments on those morbid parts for which they are indicated.

A proposal has lately emanated from high quarters, to the effect that a systematic and careful investigation should be made on the physiological action of medicines on the system. The importance of this proposal cannot be over-estimated. We may expect from its adoption the most beneficial results. In particular, we may expect to see existing discrepancies among observers swept away, and more or less uniformity substituted. We may hope that by this means the profession will be brought to a more accurate knowledge of the physiological or toxic effects of drugs on the living body. But I expect much more from the investigation than the proposers probably have dreamt of. When the physiological effects of a medicine are fairly established, they will become a guide to its

¹ Philadelphia, p. 141.

therapeutical action in those morbid conditions which are attended with dilatation of the bloodvessels (paralysis of sympathetic). We shall know then, that in such conditions its remedial action is the reverse of its toxic; and, moreover, that the dose required for the former action must be much less than for the latter. And then another field of observation has to be entered upon. We shall have to inquire what is the therapeutical dose of each medicine, the physiological dose of which we already know. As already stated, this can only be done by experiments on diseased nerves. Here is a field for experiment, so wide, so interesting, so promising, that when once entered upon, it will be cultivated with an eagerness and assiduity which no other field of science can be, and which will yield such a harvest of practical good as will throw into the shade the results of other branches of medical science. The result to therapeutics will be something like the following: each medicine will be found to irritate or cause determination of blood to that part of the system for which it has a special affinity originally, whatever may be the subsequent effects; and in morbid conditions, where such determination of blood is one of the chief symptoms, the medicine having an affinity for the affected part will prove to be the remedial agent in doses much smaller than are required for its toxic effects.

I have thus endeavoured to show that inflammation and medicinal action are identical in their primary origin, and that the administration of drugs must be regulated accordingly. What bearing these views have on other morbid conditions, I must not inquire into at present, but leave for future consideration.¹

The question will naturally arise, Do these therapeutical views not favour Homœopathy? If by that term be understood the principles and practice of the followers of Hahnemann, so far from these receiving encouragement from what I have stated, I am persuaded that when the double action of medicines is universally recognised and acted upon, the props and stay of Homœopathy will be cut away. But if the term be taken in its literal signification, the principles laid down most certainly give countenance to it. There can be no doubt that, with all its absurdities, Homœopathy contains a

¹ Since these views were matured, I have come upon the doctrines of Broussais, to which they have some resemblance. Although Broussais' opinions are now very properly abandoned, there is, nevertheless, a germ of truth in them. His idea that irritation was an essential feature of all diseases, is not so far wrong, if we limit it to those accompanied by determination of blood to the affected part. That dilatation of bloodvessels or paralysis of the sympathetic does exist primarily in many morbid states, there can be no doubt; that medicines act primarily in a similar way is also certain. Whatever remedial influence, then, is to be expected from medicines, it will be exercised by contracting the bloodvessels. This is true, notwithstanding the variety of morbid causes. In the case of simple inflammation, the medicines will be directly curative; but in specific diseases, the contraction of bloodvessels either will not take place, or if it does, no effect will be produced on the disease, or its course will be merely modified. Broussais does not appear to have had any proper idea of the application of his views to practice.

germ of truth. That germ is its original dictum of *similia similibus curantur*.¹ Hahnemann's double error, in which he has been exceeded even to extravagance by his disciples, consisted in making that dictum universally applicable to all diseases, and in pushing the small dose to infinitesimals. Had he stopped where he began, there would have been an end of all controversy. But when he developed his extraordinary opinions, and intelligent minds had naturally revolted from a system so absurd, they recoiled also from the truth out of which it sprang. Hence the doctrine of similars came to be, as it is now almost always, associated and confounded with infinitesimalism. The two, however, are essentially distinct. On the other hand, our error has been to push the principle of *contraria contrariis* to a corresponding extreme. The truth, I apprehend, lies midway between these two extremes. It is this middle position that I am endeavouring to establish. Let the homœopaths abandon, as many of them are doing, their wild theories of potentization and infinitesimalism, agreeing to receive the principle of *contraria contrariis* as having a certain range of application, and let us abandon our corresponding exclusiveness, adopting the principle of *similia similibus* where it is indicated by the pathology: let this take place, and we should have agreement upon a rational system of therapeutics. It must come to this sooner or later; for, after all, the doctrines of Hippocrates are still as true as they were on the day of their first declaration—some diseases are cured by medicines which produce the opposite effects, and some diseases are cured by medicines which produce the same effect.

In looking over the medical literature of the past few years, it is curious to notice how unconsciously homœopathic is the practice of the profession in the literal sense of *similia similibus curantur*. Let us take the theory of substitution advocated by Trousseau, and named Homœopathy by him. On this theory he proposes to cure existing inflammations by substituting, through the agency of irritants, a milder and more tractable inflammation, e.g., nitrate of silver for ophthalmia, saline purgatives for diarrhoea, etc. The principle, he says, is that the irritant drug creates an inflammation which is milder and more curable than the original. It does not appear from Trousseau's writings that he had any idea of the pathological reasons for his theory. He seems to have acted on it empirically. The explanation, however, is easy. [See diagram.] By such means, an irritant medicine acting on the nerves in the condition represented by *d* (paralysis of sympathetic and dilatation of bloodvessels) would bring them to the opposite state, and being administered in toxic or physiological doses, would elevate the nerves as far as *c* (excitement of sympathetic and contraction of

¹ I use the term here for convenience, and not as recognising it to be a scientific law. The medicines given as I recommend really act on the principle of *contraria contrariis*, and can only be regarded as acting homœopathically in respect of their physiological action.

bloodvessels). Reaction would take place to *d* again, which would now represent the new and milder artificial inflammation, from which recovery more readily takes place. Now, experience proves, as in the case of silver in ophthalmia and purgatives in diarrhoea, that by such treatment the symptoms are in most cases aggravated, as might be expected. Some are no doubt benefited, the operation of the medicine probably breaking up the spell under which the nerves are bound, and thus clearing the way for their natural elasticity to recover itself, but the tendency of such practice is the reverse. It comes near the truth ; and had the doses recommended been stimulating or contracting doses, the substitution theory would have been correct. It is impossible to read Trousseau's works without observing how homœopathic his practice was, in the sense of *similia similibus*, when he had to do with inflammatory disorders, thus empirically and unconsciously confirming the views I have been expounding on pathological laws. And when we examine the action of the few specifics we possess, it will be found that they exercise their remedial influence in accordance with the same principle. Mercury, the specific for syphilis, will, in large doses, produce symptoms resembling that disease. Quinine, as Cullen remarks, causes intermittent fever and cures it. Chlorate of potash, *the remedy par excellence* for ulcerative stomatitis, will, in large quantity, cause soreness of the gums and inflammation of the mouth. Bromide of potassium, so beneficial in epilepsy, will, when very freely administered, induce symptoms resembling the effects of that disease. Antimony, so valuable in pneumonia, will induce congestion of the lungs.¹ I might multiply instances, but these will, I think, suffice to show that, where dilatation of bloodvessels existed, the specific remedy has acted on the literal principle of *similia similibus curantur*, the dose empirically found to be remedial being much smaller than the physiological. We have merely to extend the principle to the more energetic medicines, whose toxic effects are manifested by comparatively minute doses, such as strychnia, arsenic, aconite, etc. The question for us is, how small a dose of these will contract the bloodvessels, *and no more*, when so small a quantity, comparatively, will induce both contraction and dilatation.

If, then, the foregoing views, be correct, as daily experience convinces me they are, they will tend to reconcile many conflicting therapeutical opinions, and simplify the treatment of disease in so far as medicinal agency is concerned. I have no wish to push their application beyond their proper limits, or to claim for them more success in practice than they deserve ; but I do say, that whatever benefit contraction of bloodvessels may be expected to produce in

¹ A singular confirmation of these opinions has been lately promulgated. Dr Gairdner declares that the beneficial effect of antimony in pneumonia ceases on the development of its physiological symptoms, and that the remedial doses must therefore be much less. We find also, in Grave's Clinical Medicine, a similar statement regarding antimony as a tonic in dyspepsia.

the treatment of disease, the administration of medicines on these principles will certainly effect it. The conclusions to which I have arrived are these:—

1. Whatever may be the ultimate and varied effects of medicines on the system, their primary action is analogous to the primary steps of the inflammatory process, namely, excitement of the sympathetic (contraction of bloodvessels), followed by paralysis (dilatation of bloodvessels).¹

2. The variety in the symptoms produced by the different medicines are due, partly at least, to the local tissues or nerves for which they severally have an affinity.

3. In diseases attended with a dilated condition of the blood-vessels, the proper medicines to administer are those which act physiologically on the affected part, and the dose must be such as will do no more than excite contraction of the dilated vessels (stimulus of sympathetic).

4. In so far as the dose proper to such conditions is unknown, it is to be determined by experience, and by observation on the paralyzed vaso-motor system.

In my next communication, I shall bring forward the results of my experience.

¹ It is of no consequence what view we take of the very incipient act of inflammation, whether the nerves or the molecules, as Lister has it, are first affected, the result is the same—the blood is driven back, and the vessels contracted.



